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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,192	09/25/2006	Mette Gronborg	50721/006002	5685

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	**PAPER NUMBER**
1649	

NOTIFICATION DATE	DELIVERY MODE
10/18/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/594,192	GRONBORG ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *92 and 129-131* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *92 and 129-131* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed 12/23/09 has been entered.

2. The rejection of claim 105 under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility for the recitation of "preventing apoptosis…" is withdrawn due to the cancellation of the claim.

3. The rejection of claims 93-94, 98-106 & 128 under 35 U.S.C. 112, first paragraph, for lack of proper written description rejection is withdrawn due to the cancellation of these claims.

4. The rejection of claims 93-94, 98-106 & 128 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn due to the cancellation of these claims.

5. The rejection of claims 93, 94, 100, 102 & 103 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn due to the cancellation of the claims.

6. The rejection of claims 92-94, 98-106 & 128 under 35 U.S.C. 102(b) as being anticipated by Innogenetics N.V. (WO 01/39786; IDS Ref # B2) is withdrawn due to the cancellation or amendment of the claims to now require treating Huntington's disease or neuropathic pain, versus treating MS patients.

7. The rejection of claims 93-94, 98-106 & 128 under 35 U.S.C. 102(b) as being anticipated by Tang et al/ HYSEQ, INC (WO 01/57190; IDS Ref # B6) is withdrawn due to the cancellation of these claims.

8. Applicant's arguments filed 12/23/09 have been fully considered but they are not deemed to be persuasive.

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 92 & 130-131 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons made of record in Paper No: 20090618, and as follows. This is a written description rejection.

Applicants argue on pages 4-5 of the response concerning Example 10 of the Written Description Guidelines Revision 1. In contrast, the claims are directed to "treating a neurodegenerative disorder…", which the variant proteins of SEQ ID NO: 4 must accomplish. However, as previously made of record, one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of polypeptides required to be used in the claimed method, as encompassed by claim 92 (i.e., as it relates to "at least 95% identity"), wherein only cysteine residues putatively involved in

stabilizing the 3-dimensional structure of any protein are defined. In contrast, no other polypeptides with any functionally definable characteristics are described. In other words, the specification fails to describe a single critical amino acid residue required for any definable function in the claimed genus.

Analogous to the situation decided in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), "an adequate written description of a DNA [product] requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA [product] itself".

Accordingly, the court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is".

and that:

"A description of a genus of cDNAs [products] may be achieved by means of a recitation of a representative number of cDNAs [products], *defined by nucleotide sequence*, failing in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

In contrast, an invitation for others to discover a representative number of species, in order to reasonably extrapolate to the claimed genus, with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics has not been provided within the instant specification. Thus, Applicants are clearly not in possession of

the claimed genus of NsG33 polypeptides required to practice the currently claimed method, and for the reasons previously made of record. See again MPEP 2163.

11. Claims 92 & 129-131 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a definable population of neurons with a structurally and functionally definable NsG33 polypeptide, does not reasonably provide enablement for treating unknown functions in unknown neuronal populations in patients with Huntington's disease or neuropathic pain using structurally and functionally undefined NsG33 polypeptides (i.e., as it relates to "at least 95% identity…"), or biologically functional equivalents thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record in Paper No: 20090618, and as follows.

Applicants argue on pages 5-8 of the response that "NG33 is expressed at high levels in the central midbrain in the putatmen (see Example 5), and the degeneration of these neuronal populations are associated with Huntington's disease". In contrast to Applicants' assertions, there exists more than one population of neurons in the putatmen, and Huntington's disease is characterized additionally by dysfunctional neurons in other areas of the brain (e.g., substantia nigra, neocortex, hypothalamus, thalamus, cerebellum, etc). Moreover, the specification fails to identify those specific neuronal population where the mutated Huntingtin protein is expressed (which characterizes Huntington's disease) and importantly fails to disclose how Huntingtin is associated with NsG33, if at all. Nevertheless, the issue of enablement is complicated by the fact

that the actual biological functions of the toxic Huntingtin protein itself is unclear in the art, and further not disclosed within the instant specification; especially as it relates to any undefined functional property of a variant NsG33 protein (i.e., as it relates to claims 93 & 130). As previously made of record, no actual administration of any NsG33 polypeptide, or fragment thereof, is disclosed. Examples 8-12 then invite others to experiment to see if other neuronal populations may be responsive to NsG33. No specific populations of neurons that contain receptors responsive to NsG33 are disclosed, except for possibly rat striatal neurons (and non-neuronal astrocytes after-the-fact). *In arguendo,* the claims do not recite a method of increasing the survival of striatal neurons in a Huntington's disease patient, as argued on page 6 of the response, even if basis for such a claim limitation can be found within the instant specification. In regards to Applicants' arguments regarding Jorgensen and Nishino, Jorgensen and Nishino were both published after the claimed priority date, and are alternatively directed to "activating nearby satellite glia" within the sensory ganglia, and affecting astrocyte formation/differentiaion (e.g., see Abstract of Nishio). Accordingly, the court in *In re Hogan and Banks*, 194 USPQ 527 (1977), makes clear that "enablement must be established in the specification *at the time of filing* and is to be *commensurate in scope* with the stated claims [emphasis added]".

Second, the specification fails to describe how neuropathic pain is envisioned to be treated. As argued by Applicants' on page 6 of the response, "neuropathic pain is associated with sympathetic postganglionic fiber sprouting in the dorsal rot ganglion" (see Todoroki et al.; Abstract). In contrast to Applicants' arguments on page 7 of the response, the PC12 assay described within the specification on pages 15-16 is directed toward inducing PC-12 differentiation and survival. Likewise, the specification discloses putative neurite sprouting of

PC12 cells, which when taken with the teachings of Todorski and Nishio (after-the-fact), would alternatively compound the problem of treating neuropathic pain due to "sprouting", versus resolving/treating neuropathic pain by some unknown mechanism; thereby, leaving the skilled artisan with no guidance on how to treat neuropathic pain (i.e., no sympathetic postganglionic fiber sprouting") without requiring undue experimentation to determine otherwise; especially as it relates to using variant NsG33 polypeptides, consistent with the teachings of Rudinger previously made of record.

12. Claims 92, 129 & 131 stand rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al/ HYSEQ, INC (WO 01/57190; IDS Ref # B6), for the reasons made of record in Paper No: 20090618, and as follows.

Applicants argue on pages 8-9 of the response that "WO 01/57190 does not expressly teach all active steps of the present invention". In contrast to Applicants' assertions Tang et al teach the only recite active step of "administering to the subject", wherein the patient population to be administered includes those with "lesions of …[the] peripheral nervous systems". In that Applicants' previous arguments clarifies that "neuropathic pain is associated with sympathetic postganglionic fiber sprouting in the dorsal rot ganglion", which by definition would occur during aberant sprouting following lesions in the peripheral nervous system normally, the patient population of Tang would necessarily be exposed to neuropathic pain, as claimed.

In summary, Tang et al teach administering the polypeptide of SEQ ID NO: 1401, which is 100% identical to SEQ ID NO: 4 of the instant invention (e.g., see pgs 4-5, 29 & 65-66), to treat pathological nervous system disorders, which include "lesions of either the central

(including spinal cord, brain) or peripheral nervous systems", and which also includes treating traumatic brain injury, ischemic lesions/stroke, infectious lesions, Parkinson's Disease, Alzheimer's Disease, amyotrophic lateral sclerosis, diabetic neuropathy, neurological lesions associated with metabolic and vitamin B12/folic acid deficiency, alcoholism or toxic injury, multiple sclerosis, etc. (e.g., pgs. 59-60; as it relates to claims 92, 129 & 131). In that administration of Tang's polypeptide inherently affects apoptosis, and enhances survival of the associated affected neuron populations after administration and exposing the neurons of the CNS and PNS to Tang's polypeptide, the limitations of claims 105, 106 and 128 are further anticipated. It is noted that the sole method step recited in the claims is "administering" and "exposing said neuronal cell", which Tang et al. clearly teach.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Robert C. Hayes/, Ph.D.
Primary Examiner, Art Unit 1649
October 1, 2010